

In the Claims

1 (currently amended). A method for the identification and/or quantification of one or more proteins derived from the proteome of a cell in a sample containing a mixture of such proteins, wherein said method comprises the steps of:

- a) providing a sample which contains a mixture of proteins;
- b) providing a reagent for the analysis of peptides wherein the reagent has the general formula

A-Y-PRG

in which

A constitutes at least one functional group for the reversible, covalent or non-covalent binding to a support material,

Y is a group comprising at least one chelate function for metals, and comprising a metal ion bound thereto wherein the metal is selected from the group consisting of Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La, Li, Lu, Mn, Na, Nd, Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tm, V, W, Y, Yb and Zn; and

PRG is a reactive group for the selective binding to peptides or other biomolecules to be analyzed; and wherein the arrangement of A, Y, and PRG is interchangeable and said reagent is not isotopically labeled;

- c) chemically or proteolytically cleaving the proteins in the sample in order to produce peptides;
- d) coupling the peptides to the reagent of step b) wherein the peptides are labeled by the reagent;
- e) selecting the peptides labeled in step d) using a functional group for the reversible, covalent or non-covalent binding to a support material and removal of unbound peptides;
- f) releasing the bound peptides from the support material and elution from the matrix; and
- g) detecting and identifying the labeled peptides by means of mass spectrometry.

2 (previously presented). The method, according to claim 1, wherein the cleavage of the peptides is performed enzymatically by a proteolytic enzyme.

3 (previously presented). The method, according to claim 1, wherein the labeled peptides, after their release from the support material and before their analysis by mass spectrometry, are separated from each other by means of HPLC.

4 (previously presented). The method, according to claim 1, characterized in that several protein- and/or peptide-containing samples are analyzed together.

5 (previously presented). The method, according to claim 1, further comprising the sequencing of the labeled peptides.

6 (currently amended). A method for the detection of the relative expression of proteins in a protein-containing sample, wherein said method comprises the steps of:

- a) providing a biological sample which contains proteins;
- b) providing a reagent for the analysis of peptides wherein the reagent has the general formula

A-Y-PRG

in which

A constitutes at least one functional group for the reversible, covalent or non-covalent binding to a support material,

Y is a group comprising at least one chelate function for metals, and comprising a metal ion bound thereto wherein the metal is selected from the group consisting of Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La, Li, Lu, Mn, Na, Nd, Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tm, V, W, Y, Yb and Zn,

PRG is a reactive group for the selective binding to peptides or other biomolecules to be analyzed and said reagent contains no isotopes; and wherein the arrangement of A, Y, and PRG is interchangeable and said reagent is not isotopically labeled;

- c) chemically or proteolytically cleaving the proteins in the sample in order to produce peptides;
- d) coupling the peptides to the reagent of step b) wherein the peptides are labeled by the reagent;
- e) selecting the peptides labeled in step d) utilizing a functional group for the reversible, covalent or non-covalent binding to a support material and removal of the unbound peptides;
- f) releasing the bound peptides from the support material and elution from the matrix;
- g) detecting and identifying the labeled peptides by means of mass spectrometry; and
- h) measuring the relative occurrence of the differently labeled peptides as distinct peaks of ions in order to determine the relative expression of the protein, from which the affinity-labeled peptide is derived.

7 (canceled).

8 (previously presented). The method, according to claim 6, characterized in that the labeled peptides are detected by means of a tandem technique selected from the group consisting of matrix-assisted laser desorption/ionization (MALDI), time-of-flight (TOF)-TOF-MS and electrospray ionization (ESI)-MS.

9-21 (canceled).

22 (previously presented). The method according to claim 1, wherein said mixture of proteins has not been labeled with an isotope.

23 (canceled).

24 (previously presented). The method according to claim 1, wherein the PRG group is selected from the group consisting of sulfhydryl-reactive groups, amine-reactive groups and enzyme substrates.

25 (previously presented). The method according to claim 24, wherein the PRG group is selected from the group consisting of amine-reactive pentafluorophenyl ester groups, amine-reactive N-hydroxysuccinimide ester groups, sulfonylhalides, isocyanates, isothiocyanates, active esters, tetrafluorophenyl esters, acid halides, acid anhydrides, homoserine lactone-reactive primary amine groups, carboxylic acid-reactive amines, alcohols, 2,3,5,6-tetrafluorophenyltrifluoro-acetates, iodine acetylamide groups, epoxides, α -haloacyl groups, nitriles, sulfonateds alkyls, arylthiols and maleimides.

26 (previously presented). The method according to claim 1, wherein A is selected from the group consisting of biotin, modified biotin, 1,2-diols, glutathiones, maltoses, nitrilotriacetic acid groups, oligohistidines and haptens.

27 (previously presented). The method according to claim 1, further comprising a linker between the groups A, Y and/or PRG that is cleavable.

28 (previously presented). The method according to claim 27, wherein the linker contains a disulfide group.

29 (previously presented). The method according to claim 6, wherein said mixture of proteins has not been labeled with an isotope.

30 (previously presented). The method according to claim 6, wherein the PRG group is selected from the group consisting of sulfhydryl-reactive groups, amine-reactive groups and enzyme substrates.

31 (previously presented). The method according to claim 30, wherein the PRG group is selected from the group consisting of amine-reactive pentafluorophenyl ester groups, amine-reactive N-hydroxysuccinimide ester groups, sulfonylhalides, isocyanates, isothiocyanates, active esters, tetrafluorophenyl esters, acid halides, acid anhydrides, homoserine lactone-reactive primary amine groups, carboxylic acid-reactive amines, alcohols, 2,3,5,6-tetrafluorophenyltrifluoro-acetates, iodine acetylamide groups, epoxides, α -haloacyl groups, nitriles, sulfonateds alkyls, arylthiols and maleimides.

32 (previously presented). The method according to claim 6, wherein A is selected from the group consisting of biotin, modified biotin, 1,2-diols, glutathiones, maltoses, nitrilotriacetic acid groups, oligohistidines and haptens.

33 (previously presented). The method according to claim 6, further comprising a linker between the groups A, Y and/or PRG that is cleavable.

34 (previously presented). The method according to claim 33, wherein the linker contains a disulfide group.

35 (new). The method according to claim 1, wherein Y is selected from the group consisting of macrocyclic lanthanoid chelate complexes, functionalized tetraaza-macrocycles, polyaza-polyacetic acids, DOTA, DOTA-derivatives, NOTA, NOTA-derivatives, 1,4,7,10,13,16,19,22-octaazacyclotetracosane-1,4,7,10,13,16,19,22-octaacetic acid (OTEC), 1,4,7,10,14-17,20,23-octaazacyclohexacosane-1,4,7,10,14,17,20,23-octaacetic acid (OHEC), EDTA, DTPA-BP, DTPA, DO3A, HP-DO3A and DTPA-BMA.

36 (new). The method according to claim 6, wherein Y is selected from the group consisting of macrocyclic lanthanoid chelate complexes, functionalized tetraaza-macrocycles, polyaza-polyacetic acids, DOTA, DOTA-derivatives, NOTA, NOTA-derivatives, 1,4,7,10,13,16,19,22-octaazacyclotetracosane-1,4,7,10,13,16,19,22-octaacetic acid (OTEC),

1,4,7,10,14-17,20,23-octaazacyclohexacosane-1,4,7,10,14,17,20,23-octaacetic acid (OHEC), EDTA, DTPA-BP, DTPA, DO3A, HP-DO3A and DTPA-BMA.

37 (new). The method according to claim 35, wherein Y is a macrocyclic lanthanoid chelate complex.

38 (new). The method according to claim 36, wherein Y is a macrocyclic lanthanoid chelate complex.